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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

GAKH, YELENA G

ART UNIT	PAPER NUMBER
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1743

DATE MAILED: 11/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/038,600

Applicant(s)

LEE, TU

Examiner

Yelena G. Gakh, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 January 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☒ Claim(s) 9 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 08 January 2002 is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Drawings

1. Figure 5 is objected to under 37 CFR 1.83(a) because it fails to represent the phase diagram in a proper form. It does not show a calibration of x and y axis or limits for the ratio values. Since the ratio may go only from 0 to 1 (or 0% to 100%), it is not clear, why the x-axis does not have this limit. The specification does not adequately disclose how such phase diagram can be obtained, and therefore it is not clear, what this diagram represents. It does not show different phases, and it is not clear from the drawings, which phases may be represented on the diagram. MPEP § 608.02(d). A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

2. The captions of the drawings do not reflect the subject matter of the invention, since it is not clear, which of the micrographs can be considered the one when maximum dissolution occurs and the one when maximum crystallization occurs, which are crucial for the method claimed.

Specification

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: "CHEMICAL SCREENING METHOD FOR SOLID DISPERSION SYSTEMS".

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. It is not clear from the specification, how dissolution or crystallization properties of the active compounds can be determined from the morphology of films, which seems to be the only

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characteristic of the solid dispersion system evaluated by microscopy. No dissolution studies are conducted on the films obtained on silicon wafer chips. Does it mean that the morphology of the films directly reflect the dissolution and crystallization characteristics of the system, which therefore are independent on the solvent used, the rate of evaporation and other parameters, which usually consider important for dissolution properties of the solid dispersions? It is also not clear from the specification, which phases are considered in a definition of a "phase diagram": those of the active compound and the carrier, or of the solid active component/carrier system and its solution? It looks like only the "solid solution" "phase diagrams" are obtained by the method; however, the "solid solution" is not disclosed in the specification, which makes it unclear, which systems the phase diagrams describe. Moreover, on page 8 "an equilibrium phase diagram" is disclosed. What kind of the equilibrium is expected in a dry film?

The specification discloses determination of the separation/dissolution phase boundary for the particular ratio of active ingredient by analyzing the micrographs and determining if "crystals are slightly visible against the background". This is a very vague definition of the dissolution phase boundary, since such visibility depends on the type of the instrument used, its power and resolution. Also, the disclosure does not state unambiguously that the dissolution is directly related to the degree of dispersion of the active compound in the carrier.

While Example 1 describes obtaining eight real micrographs for different sulfisoxazole/polyvinylpyrrolidone ratios, no real phase diagram was obtained for this example, and therefore the procedure of obtaining the phase diagram remains unclear. Furthermore, temperature-variable experiments should be performed for each of the ratios recited in order to obtain the phase diagram depicted on Figure 5, which was not done in any of the real examples. Therefore it is not clear, how the real phase diagram should look like for at least one real mixture, such as sulfisoxazole/polyvinylpyrrolidone.

The specification uses terms "spectrometric" and "microscopic" as synonyms, which is not quite correct, since these techniques use different principles of measurements and instrumentation, and their results, i.e. spectra and images, are not equivalent; see Webster on-line: "*spectrometer* is **1** : an instrument used for measuring wavelengths of light spectra; **2** : any of various analytical instruments in which an emission (as of particles or radiation) is dispersed according to some property (as mass or energy) of the emission and the amount of dispersion is

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measured <nuclear magnetic resonance *spectrometer*> ; *microscope* is 1 : an optical instrument consisting of a lens or combination of lenses for making enlarged **images** of minute objects; *especially* : **COMPOUND MICROSCOPE**; 2 : an instrument using radiations other than light or using vibrations for making enlarged images of minute objects <acoustic *microscope*>”.

Such misuse of the well-established terminology leads to lack of clarity and definitiveness of the specification.

Claim Objections

6. Claim 9 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 9 recites preparation of solutions through conventional laboratory methods, which does not imply any limitations to the method, since all solutions are prepared by conventional laboratory methods, which can be manual or automated.

7. Since the method is directed toward chemical screening of solid dispersion systems, the examiner suggests changing the preamble of independent claims to “a chemical screening method for solid dispersion systems”.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for obtaining morphology of the films and extent of dispersion of an active compound in a carrier, does not reasonably provide enablement for determining dissolution and crystallization properties of the solid dispersions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the

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invention commensurate in scope with these claims. No dissolution studies which can provide information on such properties, are disclosed in the specification, and therefore the specification does not enable anyone of ordinary skill in the art to use the method claimed for the purpose of screening the solid dispersion systems for their dissolution and crystallization properties.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

11. Claims 1-2, 8-9, 17-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the last step recites determining "at least the solution of the molar weight ratio", which is a technically incorrect expression. It should be rewritten as "at least the solution **with** the molar weight ratio". Moreover, if both, the maximum dissolution and crystallization should be determined, these should be two different solutions, as these are the opposite events. Also, it is not clear, how the maximum dissolution can be obtained from the micrograph of the dry film?

Claim 2 recites that the spectrometric instrument is selected from the group of microscopes, which is technically incorrect, since microscopes are not spectrometers, and vice versa.

In claims 8, 17, and 18 the term "spectroscopy" is not clear and is not definite in the context of the claim. Which spectroscopy is meant here? Also, in claim 17 it is not clear what the term "dielectric" refers to.

Conclusion

12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. *Sung et al. (Book of Abstracts, ACS Meeting, 1996)* disclose "phase separation in thin film polymer blends with and without block copolymer additives" with the films obtained on silicon wafers and analyzed by optical microscopy; *Lu et al. (Science, 1997)* disclose "nondestructive imaging of dielectric-constant profiles and ferroelectric domains with a

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scanning-tip microwave near-field microscope"; *Hobbs et al. (J. Polymer Sci., 1999)*
"experimentally determined temperatures-concentration phase diagrams of monodisperse alkanes
with chains containing between 100 and 200 carbons"; *Xiang (Annu. Rev. Mater. Sci.)* teaches
"combinatorial materials synthesis and screening: an integrated materials chip approach to
discovery and optimization of functional materials"; *Meredith et al. (Macromolecules, 2000 and
Book of Abstracts, ACS Meeting 2000)* review "combinatorial materials science for polymer thin-
film dewetting" and teach "combinatorial measurements for polymeric coatings"; *Raghavan et
al. (Macromolecules, 2000)* disclose "mapping polymer heterogeneity using atomic force
microscopy phase imaging and nanoscale indentation"; *Russek et al. (IEEE Trans., 2001)* disclose
"magnetic combinatorial thin-film libraries".

Any inquiry concerning this communication or earlier communications from the
examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (703) 306-
5906. The examiner can normally be reached on 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's
supervisor, Jill A. Warden can be reached on (703) 308-4037. The fax phone number for the
organization where this application or proceeding is assigned is (703) 872-9310.

Any inquiry of a general nature or relating to the status of this application or proceeding
should be directed to the receptionist whose telephone number is (703) 308-0661.

Yelena G. Gakh

11/6/03

